Appl. No. 09/747,760
Amdt. dated August 19, 2003
Examining Group 1639

PATENT

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) A method of screening drug candidates comprising:

a) providing a B-cell that expresses one or more expression profile genes selected from the group consisting of Egr-1 , Egr-2, Nur77, c-myc, MIP-1a (macrophage inflammatory protein-1-alpha), MIP-1b (macrophage inflammatory protein-1-alpha), BL34 (B-cell activation protein BL34), gfi-1, NAB2 (NGFI-A binding protein 2), neurogranin, SLAP (Src-like adapter protein), A1, E2-20K , SATB1, Cctq (cytosolic chaperone containing TCP-1, theta subunit), kappa V, pcp-4, TGIF, CD83 (CD83 antigen precursor), ApoE (apolipoprotein E), Aeg-2 (acidic epididymal glycoprotein-like protein-2), CD72, cyclin D2, lck, MEF-2C (myocyte-specific enhancer factor 2C), bmk (B cell/myeloid kinase), IgD (immunoglobulin D), Evi-2 (ecotropic viral intetration site 2), vimentin, CD36, c-fes, c-fos, TRAP (acid phosphatase type 5), hIP30 (gamma-interferon-inducible protein precursor), Ly6E.1, LRG-21, Fos B, gadd153, mafK, Ah-R (arylhydrocarbon receptor), C/EBP beta (CCAAT/enhancer binding protein), EZF (epithelial zinc-finger protein), TIS7, TIS11, TIS11b, LSIRF (lymphoid-specific interferon regulator factor), MKP1, PAC-1 (musculus protein tyrosine phosphatase PAC-1), PEP (protein tyrosine phosphatase), MacMARCKS, SNK (serum inducible kinase), Stra13, kir/gem, EB12 , IL1-R2 (type II interleukin-1 receptor), MyD116 (myeloid differentiation primary response), RP105 (leucine-rich repeat protein 105), uPAR (urokinase-type plasminogen activator receptor), 4F2, hRab30, Id3, BKLF, LKLF (Kruppel-like factor LKLF), EFP (estrogen-responsive finger protein), bcl-3, caspase 2, GILZ (glucocorticoid-induced leucine zipper), hIFI-204, hRhoH (RHO-related GTP-binding protein), TRAF5, LT-beta (musculus lymphotoxin-beta), IFNg-RII (interferon gamma receptor second chain), gadd45, CDC47, NAG (N-acetylglucosaminyltransferase), scd2 (stearoyl-CoA desaturase), kappa 0 ig (kappa immunoglobulin germ line gene), iap38 (immunity associated protein 38), G7e, B29, carb anh II (carbonic anhydrase II) and Stat1;

b) adding a drug candidate to the B-cell; and

Appl. No. 09/747,760
Amdt. dated August 19, 2003
Examining Group 1639

PATENT

c) determining ~~the effect of the drug candidate on~~ the expression <u>level</u> of the one or more expression profile gene<u>s in the cell;</u>

<u>d) comparing the expression level of at least one gene of the one or more expression profile genes in the cell with the expression level of the at least one gene in a control cell not contacted with the drug candidate; and</u>

<u>e) identifying the drug candidate as a potential immunosuppressant or as a potential modulator of B cell activation or B cell tolerance if a difference in the expression level of the at least one gene is determined in the comparison of step d).</u>

2-21. (Canceled)

22.   (New) The method of claim 1, wherein the expression level is determined from the amount of transcript expressed by the at least one gene.

23.   (New) The method of claim 1, wherein the expression level is determined from the amount of protein expressed by the at least one gene.

24.   (New) The method of claim 1, wherein the cell is a B cell.

25.   (New) The method of claim 24, wherein

determining comprises determining the expression level of carb anh II, IgD, CD72, SATB1, ApoE, CD83, cyclin D2, Cctq, MEF-2C, TGIF, Aeg-2, lck, E2-20K, pcp-4, kappa V, neurogranin, NAB2, gfi-1 hIP-30, TRAP, bmk, CD36, Evi-2, vimetin, Ly6E.1 and/or c-fes; and

the drug candidate is identified as a potential modulator of B cell tolerance if a difference in expression level is determined in the comparison of step d).

26.   (New) The method according to claim 25, wherein

determining comprises (i) determining whether expression of carb anh II, CD72, SATB1, ApoE, CD83, cyclin D2, Cctq, MEF-2C, TGIF, Aeg-2, lck, E2-20K, pcp-4, kappa V, neurogranin, NAB2 and/or gfi-1 is increased in the test cell relative to the control cell, or (ii) determining whether expression of Ly6E.1, vimentin, hIP-30, TRAP, bmk, CD36, Evi-2 and/or c-fes is decreased in the test cell relative to the control cell; and

Appl. No. 09/747,760
Amdt. dated August 19, 2003
'Examining Group 1639

PATENT

the drug candidate is identified as a potential modulator of B cell tolerance if the expression level of a gene listed in (i) is increased and/or the expression level of a gene listed in (ii) is decreased.

27.   (New) The method according to claim 24, wherein

determining comprises determining the expression level of NAB2, mafK, LRG-21, Stra13, AhR, gadd153, C/EBP beta, TIS11b, TIS11, gfi-1, EZF, Nur77, SNK, PAC-1, kir/gem, MacMARCKS, PEP, MKP1, hRab30, MIP-1b, MIP-1a, EB12, BL34, IL1-R2, TIS7, MyD116, uPAR, RP105, Evi-2 4F2, CD72, Id3, BKLF, EFP, Stat1, bcl-3, hRhoH, TRAF5, SLAP, LT-beta, IFNg-RII, GILZ, Caspase 2, gadd45, CDC47, NAG, scd2, kappa 0 ig, B29, iap38, G7e and/or hIFI-204; and

the drug candidate is identified as a potential B cell activator if a difference in expression level is determined in the comparison of step d).

28.   (New) The method according to claim 27, wherein

determining comprises determining whether (i) the expression of NAB2, mafK, LRG-21, Stra13, AhR, gadd153, C/EBP beta, TIS11b, TIS11, gfi-1, EZF, Nur77, SNK, PAC-1, kir/gem, MacMARCKS, PEP, MKP1, hRab30, MIP-1b, MIP-1a, EB12, BL34, IL1-R2, TIS7, MyD116, uPAR, RP105, Evi-2 4F2, and/or CD72 are increased in the test cell relative to the control cell, or (ii) the expression of Id3, BKLF, EFP, Stat1, bcl-3, hRhoH, TRAF5, SLAP, LT-beta, IFNg-RII, GILZ. Caspase 2, gadd45, CDC47, NAG, scd2, kappa 0 ig, B29, iap38, G7e, and/or hIFI-204 are decreased in the test cell relative to the control cell; and

the drug candidate is identified as a potential B cell activator if the expression level of a gene listed in (i) is increased and/or the expression level of a gene listed in (ii) is decreased.

29.   (New) The method according to claim 24, wherein

determining comprises determining the expression level of kir/gem, MKP1, hRab30, AhR, IL1-R2, TIS11b, Evi-2, EB12, MyD116, MacMARCKS, MIP-1b, MIP-1a, PEP, CD72, gadd153, EZF, C/EBP beta, Stra13, mafK, LRG-21, BL34, SNK, uPAR, TIS7, PAC-1, TIS11, gfi-1, 4F2, RP105, Nur77, IFNg-RII, CDC47, EFP, TRAF5, bcl-3, hIFI-204,

Appl. No. 09/747,760
Amdt. dated August 19, 2003
Examining Group 1639

PATENT

hRhoH, caspase 2, B29, SLAP, NAG iap38, gadd45, BKLF, G7e, Id3, scd2, GILZ, Stat1, kappa 0 ig, and/or LT-beta; and

the drug candidate is identified as a potential immunosuppressant if a difference in expression level is determined for the at least one gene.

30. (New) The method according to claim 29, wherein

determining comprises determining whether (i) the expression of kir/gem, MKP1, hRab30, AhR, Il1-R2, TIS11b,Evi-2, EB12, MyD116, MacMARCKS, MIP-1b, MIP-1a, PEP, CD72, gadd153, EZF, C/EBP beta, Stra13, mafK, LRG-21, BL34, SNK, uPAR, TIS7, PAC-1, TIS11, gfi-1, 4F2, RP105, and/or Nur77 are increased in the test cell relative to the control cell, or (ii) the expression of IFNg-RII, mCDC47, EFP, TRAF5, bcl-3, hIFI-204, hRhoH, caspase 2, B29, SLAP, NAG, iap38, gadd45, BKLF, G7e, Id3, scd2, GILZ, Stat1, kappa 0 ig, and/or LT-beta, are decreased in the test cell relative to the control cell; and

the drug candidate is identified as a potential immunosuppressant if the expression level of a gene listed in (i) is increased and/or the expression level of a gene listed in (ii) is decreased.

31. (New) The method according to claim 1, further comprising performing a binding assay to determine if the drug candidate identified in step e) binds to the protein encoded by the at least one gene.

32. (New) The method according to claim 1, further comprising performing an assay to determine if the drug candidate identified in step e) modulates an activity of the protein encoded by the at least one gene.

33. (New) The method according to claim 1, wherein the expression levels of a plurality of expression profile genes are determined and compared.

34. (New) The method according to claim 33, wherein the expression levels of at least three expression profile genes are determined and compared.

35. (New) The method according to claim 34, wherein the expression levels of at least five expression profile genes are determined and compared.